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## Orally administered interferons exert their white blood cell suppressive effects via a novel mechanism.

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Interferons (IFN) have been approved for a number of clinical uses. The accepted routes of administration are intramuscular, subcutaneous, and intravenous. Recently, interferons administered by the oral route have been shown to exert a systemic effect. Oral administrations of IFN-alpha, IFN-beta, and IFN-gamma have been shown to cause a suppression of the peripheral white blood cell (WBC) count in mice. This study investigates the mechanism by which this suppression occurs. The results show that, in contrast to their intraperitoneal administration, oral administration of rHuIFN-alpha A/D or rMuIFN-gamma does not result in the presence of detectable levels of interferons in the blood. In addition, although the presence of circulating specific antibody to interferon blocks the peripheral WBC suppressive effects of intraperitoneally administered MuIFN-beta or rMuIFN-gamma, the presence of those antibodies does not block the peripheral WBC suppressive effects of the orally administered interferons. The peripheral WBC suppressive effect of orally administered rHuIFN-alpha A/D and rMuIFN-gamma can be transferred by injection of blood from oral interferon-treated donor mice to recipient mice. Recipient mice receiving plasma from donor mice showed no peripheral WBC suppression. Recipient mice receiving blood cells from donor mice showed significant peripheral WBC suppression. No effect of orally administered rHuIFN-alpha A/D on the relative percentages of lymphocytes, neutrophils, and monocytes was noted. These results indicate that the mechanism by which orally administered interferons exert their WBC suppressive effect differs from that of intraperitoneally administered interferons. WBC suppression resulting from orally administered interferons may involve cell to cell transfer of the interferons' effects, rather than the systemic distribution of the interferons in the blood. These studies further suggest that there may be a role for oral administration as a new route of interferon administration and provide a glimpse into the mechanism by which the orally administered interferons exert their systemic effects.